Ensuring that studies meet the business goals of sponsors and increase the range of treatment options available to patients and healthcare providers can be challenging when a trial must enroll subjects with a bothersome health condition and ask them to risk randomization to placebo, especially when effective treatments are available and study participation imposes potentially burdensome requirements. The project team in a study of an investigational treatment for bacterial vaginosis addressed such challenges and enabled the study to meet the sponsor’s goals.

Bioequivalence Study for a Bacterial Vaginosis Drug

Primary Outcome Measures

The proportion of subjects achieving clinical cure at the final visit, defined as:

- return to normal physiological discharge
- negative 10% potassium hydroxide whiff test
- presence of clue cells at less than 20% of the total epithelial cells observed on microscopic examination of the saline wet mount.

Brief Study Description

This three-arm, double-blind, placebo-controlled, randomized study evaluated an investigational drug versus an active comparator and placebo in females ≥18 years of age with bacterial vaginosis. The study enrolled 876 subjects at 44 US sites and had 3 visits: screening and randomization, post-treatment assessment and test of cure.

Patient Population Description

Eligible women were non-pregnant females ages ≥18 years of age with a clinical diagnosis of bacterial vaginosis at Visit 1. Exclusion criteria included having any significant medical event, an abnormal pap or high-risk HPV within 3 months of screening, evidence of vulvovaginitis other than BV at screening, or history or presence of a condition that would
jeopardize the subject safety or study validity per the investigator's opinion.

Inclusion criteria included a diagnosis of bacterial vaginosis, a negative pregnancy test, agreeing to use protocol-allowed birth control and administering study medication per the dosing requirements.

Key Risks and Corresponding Mitigations

Important considerations in this study included variability in sites' review and documentation of saline wet mount findings for confirming the diagnosis of bacterial vaginosis, the requirement for negative tests for sexually transmitted infection, and variability in the investigators' opinions as to subjects appropriate for inclusion. Additional considerations included requirements that some potential and enrolled subjects might find burdensome:

- Refraining from use of alcohol during treatment
- Refraining from vaginal sexual intercourse during treatment
- Refraining from using any intravaginal products (e.g. tampons, birth control devices) during the trial.

Risk 1: Enrollment challenges due to number of visits
Enrollment is a challenge when patients have health conditions with troublesome symptoms, there is a risk of randomization to placebo and there is also a readily available, easy-to-use treatment option.

Mitigation: To reduce the burden of trial participation and increase the enrollment rate, the sponsor combined the screening and randomization activities into a single visit.

Risk 2: High subject discontinuations due to the burden of study participation
As with enrollment, subject retention is an issue in clinical trials where there is a risk of randomization to placebo and readily available effective treatments. Subjects expressed concerns about the requirements to refrain from drinking alcohol and vaginal sexual intercourse during treatment and from the use of a wide variety of intravaginal products.

Mitigation: Investigational sites ensured that eligible patients were fully informed of requirements for trial participation and the importance of compliance.

Risk 3: Poor subject adherence to study medications and compliance with dosing procedures
Adherence was essential for the evaluation of the investigational product in relation to study endpoints.

Mitigation: To ensure compliance with dosing and appropriate application of the medicinal products, the subjects received detailed instructions during screening visits and an information sheet for reference at home.

Conclusion
Completing enrollment took 8 months at a rate of 2.48 subjects/site/month, reflecting the challenge of enrolling a population with a troublesome health condition with readily available existing treatments, risk of randomization to placebo, and potentially burdensome study obligations. The study surmounted enrollment and retention challenges and succeeded in collecting data to support the statistical analysis.

The Leading Full-Service Women’s Health CRO from Pre-IND or -IDE to Regulatory Approval and Beyond

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